

Use of porous silicon, for transferring substances such as  
nucleic acids or constructs of them, into cells;  
porous silicon coated microneedle used for direct  
injection of DNA or RNA into host cell, with application  
in gene therapy

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AB A means of transferring a substance into a cell, using porous silicon,  
is

claimed. Also claimed is a microneedle composed of porous silicon, an  
**array** of those microneedles extending away from a **support**  
, a vector used to transfer material into a cell, containing at least  
some porous silicon, and the use of porous silicon as a transfer medium,  
for introducing material into a **living cell**. These  
are used to transfer substances, particularly DNA or RNA, or constructs  
composed of DNA or RNA, into cells, for use in gene therapy. The porous  
silicon is able to locate and immobilize biological material or other  
substances to be transferred into cells, so that the transferred  
substance can combine with cellular DNA, or be released to produce an  
effect, specifically to express a recombinant protein. The porous  
silicon can be resorbed by a mammalian body without significant  
detrimental effects. The silicon can be used to produce a cell  
penetrating member with a porous tip, used to introduce the material

into

the cell. This preferably involves the use of a microneedle coated with  
a porous silicon. (32pp)

**Mitochondrial DNA sequence variation in**

human evolution and disease  
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CORPORATE SOURCE: Department of Genetics and Molecular Medicine, Emory  
University School of Medicine, Atlanta, GA, 30322, USA  
SOURCE: Proceedings of the National Academy of Sciences of the  
United States of America (1994), 91(19), 8739-46  
CODEN: PNASA6; ISSN: 0027-8424  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review with 101 refs. Germ-line and somatic mtDNA mutations are hypothesized to act together to shape our history and our health. Germ-line mtDNA mutations, both ancient and recent, have been assocd. with a variety of degenerative diseases. Mildly to moderately deleterious germ-line mutations, like neutral polymorphisms, have become established in the distant past through genetic drift but now may predispose certain individuals to late-onset degenerative diseases. As an example, a **homoplasmic**, Caucasian, tRNAGln **mutation** at nucleotide pair (np) 4336 has been obsd. in 5% of Alzheimer disease and Parkinson disease patients and may contribute to the multifactorial etiol. of these diseases. Moderately to severely deleterious germ-line mutations, on the other hand, appear repeatedly but are eliminated by selection. Hence, all extant mutations of this class are recent and assocd. with more devastating diseases of young adults and children. Representative of these mutations is a heteroplasmic **mutation** in MTND6 at np 14459 whose clin. presentations range from adult-onset blindness to pediatric dystonia and basal ganglial degeneration. To the inherited mutations are added somatic mtDNA mutations which accumulate in random arrays within stable tissues. These mutations provide a mol. clock that measures our age and may cause a progressive decline in tissue energy output that could ppt. the onset of degenerative diseases in individuals harboring inherited deleterious mutations.

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ACCESSION NUMBER: 1994:206314 BIOSIS  
DOCUMENT NUMBER: PREV199497219314  
TITLE: Defective respiratory capacity and **mitochondrial**  
protein synthesis in transformant cybrids harboring the  
tRNA-Leu(UUR) **mutation** associated with maternally  
inherited myopathy and cardiomyopathy.  
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CORPORATE SOURCE: (1) Dep. Biochem. Genet., Ist. Naz. Neurol. C. Besta, via  
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SOURCE: Journal of Clinical Investigation, (1994) Vol. 93, No. 3,  
pp. 1102-1107.  
ISSN: 0021-9738.  
DOCUMENT TYPE: Article  
LANGUAGE: English

AB We studied the physiometabolic effects of a **mitochondrial** DNA (mtDNA) heteroplasmic point **mutation**, the A fwdarw G-3260 transition associated with maternally inherited myopathy and cardiomyopathy. To eliminate the possible influence of the autochthonous nuclear gene set, we fused myoblast-derived cytoplasts of a patient with a human tumoral cell line deprived of mtDNA (Rho-o). The presence and amount of the mutant G-3260 vs the wild-type A-3260 were measured by solid phase minisequencing. We observed a marked reduction of the percentage of mutant mtDNA in the culture system compared with that measured in the donor's muscle biopsy, suggesting the presence of negative selection against the **mutation**. Furthermore, stable mitotic segregation of the two mtDNA populations was observed in 18 of 19 transformant clones, suggesting the presence of intraorganelle and possibly intracellular homoplasmy in the precursor cells of the donor. Several indexes of mtDNA-related respiratory

capacity, including oxygen consumption, complex I- and complex IV-specific activities, and lactate production, were markedly abnormal in the clones containing a high proportion of mutant mtDNA, as compared with those

homoplastic A12,753G **mitochondrial** DNA

**mutation** in a Hungarian family.

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SOURCE: Acta Biologica Hungarica, (1998) Vol. 49, No. 1, pp.  
119-124.

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DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A 42-year-old male patient with clinical symptoms resembling multiple sclerosis but showing slight unusual myopathic features was referred to our clinic. Analysis of mtDNA isolated from the patient's skeletal muscle revealed two **homoplastic** Pvu II restriction sites instead of the usual single one. At the same time, digestion of the DNA with BamH I and with Sac I resulted in the normal one and two restriction fragments, respectively. For search of the **mutation** as the possible background of the patient's disease, serial PCR amplifications were carried out, and the new Pvu II site was tentatively located within the 12,352 and 12,914 np. This region of the patient's mtDNA was sequenced and an A to G transition at the 12,753 np position was found. According to the sequence analysis, this **mutation** was responsible for generation of the new Pvu II restriction site. The **mutation** caused a modification of the CAA triplet at the 12,751 position to CAG. Since both triplets encode glutamine in the mtDNA, the **mutation** could not have been responsible for the patient's disease. The same **mutation** was identified in the healthy brothers of the patient. Our investigation seems to have recognized a variant of the mtDNA in a Hungarian family which has not been revealed so far in any European haplogroup.